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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,016	GEORGE ET AL.	
	Examiner	Art Unit	
	Jason Heidemann	2624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 June 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-28 are pending

Priority

This application claims benefit of an earlier filing date under 35 U.S.C. 119(e) of a continuation of International Application No. PCT/US05/08870, filed 03/16/2005, which claims the benefit of U.S. Provisional Application 60/553,502, filed 03/16/2004.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 .S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

There is a lack of antecedent basis for limitations “using the nuclear marker image” and “the cell image”, in the claim. Examiner will interpret the claim as reciting " using a nuclear marker image " and “a cell image”, for examination purposes.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 1, 2, 3, 26/1, 26/2 and 26/3 are rejected under 35 U.S.C. 102(b) as being anticipated by Basiji et al. (US Patent # 6,211,955, hereinafter Basiji).

As to Claim 1, Basiji teaches a method for identifying a specific cell, comprising directing incident light at a cell (**Basiji, US Patent 6211955, Abstract, Column 6, Lines 15-16, a light source is diposed to provide an incident light that illuminates the object (cell)**), using a detector to obtain a side scatter image (**Basiji, 6211955, Fig. 5, Fig.6, Abstract, Column 6, Lines 15-26, Lines 43-54, a detector is used to collect the scatter image of the object, the detectors are perpendicular to the light beam (Side scatter)**), and using the spatial frequency content of the side scatter image

to identify a specific cell (**Basiji, 6211955, Column 8, Lines 24-47, Column 17, Lines 27-31, teaches using spatial frequency content to be used in cell analysis, a cell are identified using the morphogical parameters (spatial frequency content)**).

As to Claim 2, Basiji teaches the method of claim 1 wherein there is **relative motion** between the cell and the detector (**Basiji, 6211955, Column 2, Column 3, Lines 50-62, Line 49-50, Column 4, Lines 6-28, the detector captures the velocity (relative motion) between the cells and the detector**).

As to Claim 3, Basiji teaches the method of claim 1 wherein a specific cell subpopulation is identified with a **heterogeneous cell population** (**Basiji, 6211955, Abstract, Column 3, Line 62-67, Column 4, Lines 1-6**).

As to Claims 26/1, 26/2, and 26/3 they recite the same limitations as the claims they depend from, 1, 2, and 3 respectively, with the added limitation if wherein the detector is a time delay integration charge-coupled detector. Basiji further teaches a detector can be a time delay integration charge-coupled detector (**Basiji, 6211955, Abstract, Column 2, Line 35, Fig. 16, Lines 54-67**).

B. Claims 8, 9, 10, 15, 26/8, 26/9, 26/10, and 26/15 are rejected under 35

U.S.C. 102(b) as being anticipated by Ortyn et al. (US PGPub #2002/0071121, hereinafter Ortyn).

As to Claim 8, Ortyn teaches a method for identifying a specific cell, comprising directing incident light at a cell (**Ortyn, US PGPub #2002/0071121, [0029], [0030], teaches having a light source incident upon the object (cell)**), using a detector to obtain a brightfield image (**Ortyn, US PGPub 2002/0071121, [0124], [0071]**), and using the spatial frequency content of the brightfield image to identify a specific cell (**Ortyn, [0124], [0064], [0010], uses a brightfield to more accurately analyze morphological detail, where morphological parameters include (spatial frequency content))**.

As to Claim 9, Ortyn teaches the method of claim 8 wherein there is relative motion between the cell and the detector (**Ortyn, [0014], [0017], [0018], Column 4, Lines 6-28, the detector captures the velocity (relative motion) between the cells and the detector**).

As to Claim 10, Ortyn teaches the method of claim 8 wherein a specific cell subpopulation is identified with a heterogeneous cell population (**Ortyn, Abstract, [0010]**).

As to Claim 15, Ortyn teaches the method of claim 8 wherein the spatial frequency content is of the nucleus (**Ortyn, Abstract, [0064], measures spatial frequency of the nuclear area (nucleus)**)

As to Claims 26/8, 26/9, 26/10, and 26/15, they recite the same limitations as the claims they depend from, 8-10 and 15, respectively, with the added limitation if wherein the detector is a time delay integration charge-coupled detector. Ortyn further teaches a detector can be a time delay integration charge-coupled detector (**Ortyn, Abstract, [0013], [0014]**).

C. Claims 16, 17, 18, 23, 25/16, 25/17, 25/18, and 25/23 are rejected under 35 U.S.C. 102(e) as being anticipated by Rosania et al. (US PGPub # 2003/0059093 A1, hereinafter Rosania).

As to Claim 16, Rosania teaches method for identifying a specific cell (**Rosania, [0027]**), comprising contacting a cell with a **nuclear marker** (**Rosania, [0065], [0028], [0029]**), directing incident light at the marked cell (**Rosania, [0031], [0029], the light is either absorbed, reflect off a molecule, thus a (direct) light that falls on a surface, and is therefore an incident light**) using a detector to obtain an image of the cell (**Rosania, [0031], [0032], [0029], a camera is used to collect images of the data, the cellular component of interest**), and using (the) a nuclear marker image **in combination with the spatial frequency** content of (the) a cell image to identify a

specific cell (**Rosania, [0026], [0054], [0056], [0057], [0058], [0060], [0065], teaches using the nuclear image and measuring other features such as spatial frequency of the signals using a Fourier transform to identify the cell**).

As to Claim 17, Rosania teaches the method of claim 16 wherein there is relative motion between the cell and the detector (**Rosania, [0075]**).

As to Claim 18, Rosania teaches the method of claim 16 wherein a specific cell subpopulation is identified with a heterogeneous cell population (**Rosania, Fig.1, Fig. 4, [0009], [0026], [0060], the specific domain is identified with a heterogeneous cell pollutions (cells of different shapes, masses, etc), analysis is performed on the domain of interest from the identified cellular domains (subpopulations)**).

As to Claim 23, Rosania teaches the method of claim 16 wherein a single nuclear marker is used (**Rosania, [[0028], [0029], a reference component (nuclear marker) is used to allow the detected on the component of interest**).

As to Claim 25/19, 25/20, 25/21, and 25/22 the combination of Rosania and Rich teach the method according to any one of claims **19, 20, 21, and 22 respectively as applied to above,** wherein the images are collected simultaneously (**Rosania, [0005]**

[0054], [0067], [0079], [0032], [0031], the reference component image, and cellular component are collected).

E. Claims 27 is rejected under 35 U.S.C. 102(e) as being anticipated by Yaroslavsky et al. (US PGPub # 2005/0094147 A1, hereinafter Yaroslavsky).

As to Claim 27, Yaroslavsky teaches a kit for use in a multispectral imaging system to identify a specific cell type (**Yaroslavsky, Fig.1, [0045], [0052]**),comprising a single kit for use in a multispectral imaging system to identify a specific cell type (**Yaroslavsky, [0022], [0036]**) ,
wherein a cell contacted with the single marker for a time sufficient to allow identification of an apoptotic cell or a necrotic cell with the multispectral imaging system (**Yaroslavsky, [0036], [0087], [0090], [0024], [0032], [0029]**).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A.) Claims 4, 7, 26/4, and 26/7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Basiji in view of Kim et al. (US PG Pub # 2003/0040031 A1, hereinafter Kim).

As to Claim 4, Basiji teaches the method of claim 1 wherein the specific cell identified is an **apoptotic cell**. However, Basiji doesn't explicitly teach wherein the specific cell identified is an apoptotic cell.

Kim teaches identifying cell death (apoptotic cell) in a captured images of grouped of cells (**Kim, [0227]**). Kim performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Basiji, by identifying apoptotic cells as to the teaching of Kim. Basiji and Kim are analogous in the art of image based cell analysis, and Kim addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Kim to the method of Basiji in order to use the image based analysis method of Basiji to identify specific cells that include cell death (apoptotic cells) as taught by Kim to provide detection of cells that are dying.

Further, Basiji and Kim collectively teach all of the claimed elements, the teaching of Kim performs the same function in combination with Basiji as taught individually in Kim, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claim 7, Basiji teaches the method of claim 1. However, Basiji doesn't explicitly teach wherein the specific **cell identified is at least one** of an apoptotic cell and a necrotic cell.

Kim teaches at least identifying cell death (apoptotic cell) in a captured image of grouped of cells (**Kim, [0227]**). Kim performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Basiji, by identifying apoptotic cells as to the teaching of Kim. Basiji and Kim are analogous in the art of image based cell analysis, and Kim addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Kim to the method of Basiji in order to use the image based analysis method of Basiji to identify specific cells that include cell death (apoptotic cells) as taught by Kim to provide detection of cells that are dying.

Further, Basiji and Kim collectively teach all of the claimed elements, the teaching of Kim performs the same function in combination with Basiji as taught individually in Kim, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claims 26/4 and 26/7, they recite the same limitations as the claims they depend from, 1 and 2, respectively, with the added limitation if wherein the detector is a time delay integration charge-coupled detector. Basiji further teaches a detector can be

a time delay integration charge-coupled detector (**Basiji, 6211955, Abstract, Column 2, Line 35, Fig. 16, Lines 54-67**).

B.) Claims 11, 14, 26/11, and 26/14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortyn in view of Kim.

As to Claim 11, Ortyn teaches the method of claim 8 wherein the specific cell identified is an apoptotic cell. However, Ortyn doesn't explicitly teach wherein the specific cell identified is an apoptotic cell.

Kim teaches identifying cell death (apoptotic cell) in a captured images of grouped of cells (**Kim, [0227]**). Kim performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Ortyn, by identifying apoptotic cells as to the teaching of Kim. Ortyn and Kim are analogous in the art of image based cell analysis, and Kim addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Kim to the method of Ortyn in order to use the image based analysis method of Ortyn to identify specific cells that include cell death (apoptotic cells) as taught by Kim to provide detection of cells that are dying.

Further, Ortyn and Kim collectively teach all of the claimed elements, the teaching of Kim performs the same function in combination with Ortyn as taught

individually in Kim, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claim 14, Ortyn teaches the method of claim 8 wherein the specific cell identified is at least one of an apoptotic cell and a necrotic cell. However, Basiji doesn't explicitly teach wherein the specific **cell identified is at least one** of an apoptotic cell and a necrotic cell.

Kim teaches at least identifying cell death (apoptotic cell) in a captured image of grouped of cells (**Kim, [0227]**). Kim performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Ortyn, by identifying apoptotic cells as to the teaching of Kim. Ortyn and Kim are analogous in the art of image based cell analysis, and Kim addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Kim to the method of Ortyn in order to use the image based analysis method of Ortyn to identify specific cells that include cell death (apoptotic cells) as taught by Kim to provide detection of cells that are dying.

Further, Ortyn and Kim collectively teach all of the claimed elements, the teaching of Kim performs the same function in combination with Ortyn as taught individually in Kim, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claims 26/11 and 26/14, they recite the same limitations as the claims they depend from, 8 and 9, respectively, with the added limitation if wherein the detector is a time delay integration charge-coupled detector. Ortyn further teaches a detector can be a time delay integration charge-coupled detector (**Ortyn, Abstract, [0013], [0014]**).

C.) Claims 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortyn in view of Kim.

As to Claim 19, Rosania teaches the method of claim 16. However, Rosania doesn't explicitly teach wherein the specific cell identified is an apoptotic cell.

Kim teaches identifying cell death (apoptotic cell) in a captured images of grouped of cells (**Kim, [0227]**). Kim performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by identifying apoptotic cells as to the teaching of Kim. Rosania and Kim are analogous in the art of image based cell analysis, and Kim addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Kim to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells that include cell death (apoptotic cells) as taught by Kim to provide detection of cells that are dying.

Further, Rosania and Kim collectively teach all of the claimed elements, the teaching of Kim performs the same function in combination with Rosania as taught individually in Kim, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claim 22, Rosania teaches the method of claim 16. However, Rosania doesn't explicitly wherein the specific cell identified is at least one of an apoptotic cell and a necrotic cell.

Kim teaches identifying cell death (apoptotic cell) in a captured images of grouped of cells (**Kim, [0227]**). Kim performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by identifying apoptotic cells as to the teaching of Kim. Rosania and Kim are analogous in the art of image based cell analysis, and Kim addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Kim to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells that include cell death (apoptotic cells) as taught by Kim to provide detection of cells that are dying.

Further, Rosania and Kim collectively teach all of the claimed elements, the teaching of Kim performs the same function in combination with Rosania as taught

individually in Kim, and the results would be highly predictable (Identifying cell death in a cell analysis method).

D.) Claims 4, 5, 6, 7, 26/4, 26/5, 26/6, and 26/7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Basiji in view of Rich (US PGPub # 2001/0012620, hereinafter Rich).

As to Claim 4, Basiji teaches the method of claim 1 wherein the specific cell identified is an **apoptotic cell**. However, Basiji doesn't explicitly teach wherein the specific cell identified is an apoptotic cell.

Rich teaches identifying cell death (apoptotic cell) in a captured images of grouped of cells (**Rich, [0035], [052], [0065], [0132], [0133], teaches measuring the stage of an apoptotic cell**).Rich performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Basiji, by identifying apoptotic cells as to the teaching of Rich. Basiji and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Rich to the method of Basiji in order to use the image based analysis method of Basiji to identify specific cells that include cell death (apoptotic cells) as taught by Rich to provide detection of cells that are dying.

Further, Basiji and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Basiji as taught individually in Rich, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claim 5, Basiji teaches the method of claim 4. However, Basiji doesn't explicitly teach wherein the apoptotic cell is an **early stage** apoptotic cell **or** a **late stage** apoptotic cell

Rich further teaches identifying stages of cell death (apoptotic cell) in a captured images of grouped of cells (**Rich, [0035], [052], [0065], [0132], [0133], teaches measuring the stage of an apoptotic cell**).

It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of **Basiji**, by including an additional step of detecting the presence of PPS to classify the stage the apoptotic cell is in as to the teaching of **Rich**.

Basiji and **Rich** are analogous in the art of image based cell analysis, and **Rich** addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of **Rich** to the method of **Basiji** in order to use the image based analysis method of **Basiji** to identify specific cells that include cell death (apoptotic cells) as taught by **Rich** to provide detection of cells that are dying.

Further, **Basiji** and **Rich** collectively teach all of the claimed elements, the teaching of **Rich** performs the same function in combination with **Basiji** as taught individually in **Rich**, and the results would be highly predictable (Identifying the stage (early or late) of an apoptotic cell in a cell analysis method).

As to Claim 6, Basiji teaches the method of claim 1. However, Basiji doesn't explicitly teach wherein the specific cell identified is a **necrotic cell**.

Rich further teaches identifying specific cell identified is a **necrotic cell** (**Rich, [0132]**).

It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of **Basiji**, by including an additional step of detecting the necrotic cells using by counterstaining cells with propidium iodide (PI) as to the teaching of **Rich.**

Basiji and **Rich** are analogous in the art of image based cell analysis, and **Rich** addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of **Rich** to the method of **Basiji** in order to use the image based analysis method of **Basiji** to identify specific cells that include dead cells (necrotic cells) as taught by **Rich** to provide detection of cells that are dead.

Further, **Basiji** and **Rich** collectively teach all of the claimed elements, the teaching of **Rich** performs the same function in combination with **Basiji** as taught individually in **Rich**, and the results would be highly predictable (Identifying the dead cells in a cell analysis method).

As to Claim 7, Basiji teaches the method of claim 1. However, Basiji doesn't explicitly teach wherein the specific **cell identified is at least one** of an apoptotic cell and a necrotic cell.

Rich teaches at least identifying cell death (apoptotic cell) in a captured image of grouped of cells (**Rich, [0227]**). Rich performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Basiji, by identifying apoptotic cells as to the teaching of Rich. Basiji and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Rich to the method of Basiji in order to use the image based analysis method of Basiji to identify specific cells that include cell death (apoptotic cells) as taught by Rich to provide detection of cells that are dying.

Further, Basiji and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Basiji as taught

individually in Rich, and the results would be highly predictable (Identifying at least cell death in a cell analysis method).

As to Claims 26/4, 26/5, 26/6 and 26/7, they recite the same limitations as the claims they depend from, 4,5,6, and 7 respectively, with the added limitation if wherein the detector is a time delay integration charge-coupled detector. Basiji further teaches a detector can be a time delay integration charge-coupled detector (**Basiji, 6211955, Abstract, Column 2, Line 35, Fig. 16, Lines 54-67**).

E.) Claims 11, 12, 13, 14, 26/11, 26/12, 26/13 and 26/14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortyn in view of Rich.

As to Claim 11, Ortyn teaches the method of claim 1 wherein the specific cell identified is an **apoptotic cell**. However, Ortyn doesn't explicitly teach wherein the specific cell identified is an apoptotic cell.

Rich teaches identifying cell death (apoptotic cell) in a captured images of grouped of cells (**Rich, [0035], [052], [0065], [0132], [0133], teaches measuring the stage of an apoptotic cell**).Rich performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Ortyn, by identifying apoptotic cells

as to the teaching of Rich. Ortyn and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Rich to the method of Ortyn in order to use the image based analysis method of Ortyn to identify specific cells that include cell death (apoptotic cells) as taught by Rich to provide detection of cells that are dying.

Further, Ortyn and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Ortyn as taught individually in Rich, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claim 12, Ortyn teaches the method of claim 11. However, Ortyn doesn't explicitly teach wherein the apoptotic cell is an **early stage** apoptotic cell **or** a **late stage** apoptotic cell

Rich further teaches identifying stages of cell death (apoptotic cell) in a captured images of grouped of cells (**Rich, [0035], [052], [0065], [0132], [0133], teaches measuring the stage of an apoptotic cell**).

It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of **Ortyn**, by including an additional step of detecting the presence of PPS to classify the stage the apoptotic cell is in as to the teaching of **Rich**.

Ortyn and **Rich** are analogous in the art of image based cell analysis, and **Rich** addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of **Rich** to the method of **Ortyn** in order to use the image based analysis method of **Ortyn** to identify specific cells that include cell death (apoptotic cells) as taught by **Rich** to provide detection of cells that are dying.

Further, **Ortyn** and **Rich** collectively teach all of the claimed elements, the teaching of **Rich** performs the same function in combination with **Ortyn** as taught individually in **Rich**, and the results would be highly predictable (Identifying the stage (early or late) of an apoptotic cell in a cell analysis method).

As to Claim 13, Ortyn teaches the method of claim 1. However, Ortyn doesn't explicitly teach wherein the specific cell identified is a **necrotic cell**.

Rich further teaches identifying specific cell identified is a **necrotic cell** (**Rich, [0132]**).

It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of **Ortyn**, by including an additional step of detecting the necrotic cells using by counterstaining cells with propidium iodide (PI) as to the teaching of **Rich.**

Ortyn and **Rich** are analogous in the art of image based cell analysis, and **Rich** addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of **Rich** to the method of **Ortyn** in order to use the image based analysis method of **Ortyn** to identify specific cells that include dead cells (necrotic cells) as taught by **Rich** to provide detection of cells that are dead.

Further, **Ortyn** and **Rich** collectively teach all of the claimed elements, the teaching of **Rich** performs the same function in combination with **Ortyn** as taught individually in **Rich**, and the results would be highly predictable (Identifying the dead cells in a cell analysis method).

As to Claim 14, Ortyn teaches the method of claim 1. However, Ortyn doesn't explicitly teach wherein the specific **cell identified is at least one** of an apoptotic cell and a necrotic cell.

Rich teaches at least identifying cell death (apoptotic cell) in a captured image of grouped of cells (**Rich, [0227]**). Rich performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Ortyn, by identifying apoptotic cells as to the teaching of Rich. Ortyn and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine

the teachings of Rich to the method of Ortyn in order to use the image based analysis method of Ortyn to identify specific cells that include cell death (apoptotic cells) as taught by Rich to provide detection of cells that are dying.

Further, Ortyn and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Ortyn as taught individually in Rich, and the results would be highly predictable (Identifying at least cell death in a cell analysis method).

As to Claims 26/11, 26/12, 26/13 and 26/14, they recite the same limitations as the claims they depend from, 11, 12, 13, and 14 respectively, with the added limitation if wherein the detector is a time delay integration charge-coupled detector. Ortyn further teaches a detector can be a time delay integration charge-coupled detector (**Ortyn, Abstract, [0013], [0014]**).

F.) Claims 19, 20, 21, 22, 25/19, 25/20, 25/21, and 25/22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosania in view of Rich.

As to Claim 19, Rosania teaches the method of claim 16. However, Rosania doesn't explicitly teach wherein the specific cell identified is an apoptotic cell.

Rich teaches at least identifying cell death (apoptotic cell) in a captured image of grouped of cells (**Rich, [0227]**). Rich performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by identifying apoptotic cells as to the teaching of Rich. Rosania and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Rich to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells that include cell death (apoptotic cells) as taught by Rich to provide detection of cells that are dying.

Further, Rosania and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Rosania as taught individually in Rich, and the results would be highly predictable (Identifying cell death in a cell analysis method).

As to Claim 20, Rosania teaches the method of claim 19. However, Rosania doesn't explicitly teach wherein the apoptotic cell is an early stage apoptotic cell or a late stage apoptotic cell.

Rich further teaches identifying stages of cell death (apoptotic cell) in a captured images of grouped of cells (**Rich, [0035], [052], [0065], [0132], [0133], teaches measuring the stage of an apoptotic cell**). It would have been obvious to one of

ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by including an additional step of detecting the presence of PPS to classify the stage the apoptotic cell is in as to the teaching of **Rich**. Rosania and **Rich** are analogous in the art of image based cell analysis, and **Rich** addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of **Rich** to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells that include cell death (apoptotic cells) as taught by **Rich** to provide detection of cells that are dying.

Further, Rosania and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Rosania as taught individually in Rich, and the results would be highly predictable (Identifying the stage (early or late) of an apoptotic cell in a cell analysis method).

As to Claim 21, Rosania teaches the method of claim 16. However, Rosania doesn't explicitly wherein the specific cell identified is a necrotic cell.

Rich further teaches identifying specific cell identified is a necrotic cell (**Rich, [0132]**). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by including an additional step of detecting the necrotic cells using by counterstaining cells with propidium iodide (PI) as to the teaching of Rich.

Rosania and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Rich to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells that include dead cells (necrotic cells) as taught by Rich to provide detection of cells that are dead.

Further, Rosania and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Rosania as taught individually in Rich, and the results would be highly predictable (Identifying the dead cells in a cell analysis method).

As to Claim 22, Rosania teaches the method of claim 16. However, Rosania doesn't explicitly wherein the specific cell identified is at least one of an apoptotic cell and a necrotic cell.

Rich teaches at least identifying cell death (apoptotic cell) in a captured image of grouped of cells (**Rich, [0227]**). Rich performs cell analysis for identifying and analyzing cells. 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by identifying apoptotic cells as to the teaching of Rich. Rosania and Rich are analogous in the art of image based cell analysis, and Rich addresses the same problem solving area specific cell analysis. One of ordinary skilled in the art would have been motivated to combine

the teachings of Rich to the method of Rosania in order to use the image based analysis method of Rosania to identify at least one specific cells that include cell death (apoptotic cells) as taught by Rich to provide detection of cells that are dying.

Further, Rosania and Rich collectively teach all of the claimed elements, the teaching of Rich performs the same function in combination with Rosania as taught individually in Rich, and the results would be highly predictable (Identifying at least cell death in a cell analysis method).

As to Claim 25/19, 25/20, 25/21, and 25/22 the combination of Rosania and Rich teach the method according to any one of claims **19, 20, 21, and 22 respectively as applied to above,** wherein the images are collected simultaneously (**Rosania, [0005] [0054], [0067], [0079], [0032], [0031], the reference component image, and cellular component are collected**).

G.) Claim 24 and 25/24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosania in view of Fraatz (US Patent # 5372936, hereinafter Fraatz).

As to Claim 24, Rosania teaches the method of claim 16. However, Rosania doesn't explicitly teach wherein the single nuclear marker is 7-aminoactinomycin D.

Fraatz teaches using 7-aminoactinomycin D as a maker for imagining samples (**Fraatz, Column 8, Table 1, Table 2, Column 6, lines 1-20**). Fraatz performs analysis

for identifying biological activities in specimens (cells). 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identifying cells of Rosania, by using 7-aminoactinomycin D as the nuclear marker as to the teaching of Fraatz. Rosania and Fraatz are analogous in the art of image based biological analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Fraatz to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells using the nuclear marker, 7-aminoactinomycin D, since it has useful properties (fluorescent dye) that would enable the isolation of cells in the image, as taught by Fraatz.

Further, Rosania and Fraatz collectively teach all of the claimed elements, the teaching of Fraatz performs the same function in combination with Rosania as taught individually in Fraatz, and the results would be highly predictable (Identifying cell in the image using the fluorescent dye (7-aminoactinomycin D) as a nuclear maker).

As to Claim 25/24, Rosania teaches the method according to any one of claims 24 wherein the images are collected simultaneously (Rosania, [0005] [0054], [0067], [0079], [0032], [0031], the reference component image, and cellular component are collected).

H. Claims 26/16, 26/17, 26/18, and 26/23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosania in view of Basiji.

As to Claims 26/16, 26/17, 26/18, and 26/23, they recite the same limitations as the claims they depend from 16, 17, 18, and 23 respectively, with the added limitation wherein the detector is a time delay integration charge-coupled detector. However, Rosania is silent to wherein the detector is can be a time delay integration charge-coupled detector

Basiji, however, teaches a detector can be a time delay integration charge-coupled detector (**Basiji, 6211955, Abstract, Column 2, Line 35, Fig. 16, Lines 54-67**). Basiji performs analysis for identifying specific cells by collecting images using a TDI CCD. It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of Rosania, by using a time delay integration charge-coupled detector to collect images of cells as to the teaching of Basiji. Rosania and Basiji are analogous in the art of image based cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Basiji to the method of Rosania in order to use the image based analysis method of Rosania to identify specific cells using the time delay integration charge-coupled detector to collect images of cells, since it has been demonstrated as an effective instrument for acquisition of images for cell analysis as shown in Basiji.

Further, Rosania and Basiji collectively teach all of the claimed elements, the teaching of Basiji performs the same function in combination with Rosania as taught individually in Basiji, and the results would be highly predictable (Identifying cell in the images that were acquired by a time delay integration charge-coupled detector).

I. Claims 26/19, 26/20, 26/21, and 26/22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosania in view of Rich and in further view of Basiji.

As to Claims **26/19, 26/20, 26/21, and 26/22**, they recite the same limitations as the claims they depend from 19, 20, 21 ,22 respectively, with the added limitation wherein the detector is a time delay integration charge-coupled detector. Using the rejection of Claims 19, 20, 21, and 22 as rejected in Section F, with 35 U.S.C. 103(a) with the combination of Rosania and Rich. The combination of Rosania and Rich as applied to Claims 19 – 22 are all silent to wherein the detector is can be a time delay integration charge-coupled detector

Basiji, however, teaches a detector can be a time delay integration charge-coupled detector (**Basiji, 6211955, Abstract, Column 2, Line 35, Fig. 16, Lines 54-67**). Basiji performs analysis for identifying specific cells by collecting images using a TDI CCD. It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the method for identify cells of the combination of Rosania and Rich, by using a time delay integration charge-coupled detector to collect images of cells as to the teaching of Basiji. The combination of Rosania and Rich and Basiji are analogous in the art of image based cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Basiji to the method of the combination of Rosania and Rich in order to use the image based analysis method of the combination of Rosania and Rich to identify specific cells using the time delay

integration charge-coupled detector to collect images of cells, since it has been demonstrated as an effective instrument for acquisition of images for cell analysis as shown in Basiji.

Further, the combination of Rosania and Rich and Basiji collectively teach all of the claimed elements, the teaching of Basiji performs the same function in combination with the combination of Rosania and Rich as taught individually in Basiji, and the results would be highly predictable (Identifying cell in the images that were acquired by a time delay integration charge-coupled detector).

J. Claim 26/24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rosania in view of Fraatz and in further view of Basiji.

As to Claims **26/24**, it recites the same limitations as claim 24 with the added limitation wherein the detector is a time delay integration charge-coupled detector. Using the rejection of Claim 24 as rejected in Section G, with 35 U.S.C. 103(a) with the combination of Rosania and Fraatz. The combination of Rosania and Fraatz as applied to Claims 24 is silent to wherein the detector is can be a time delay integration charge-coupled detector

Basiji, however, teaches a detector can be a time delay integration charge-coupled detector (**Basiji, 6211955, Abstract, Column 2, Line 35, Fig. 16, Lines 54-67**). Basiji performs analysis for identifying specific cells by collecting images using a TDI CCD. It would have been obvious to one of ordinary skilled in the art at the time of

inventions to modify the method for identify cells of the combination of Rosania and Fraatz, by using a time delay integration charge-coupled detector to collect images of cells as to the teaching of Basiji. The combination of Rosania and Fraatz and Basiji are analogous in the art of image based cell analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Basiji to the method of the combination of Rosania and Fraatz in order to use the image based analysis method of the combination of Rosania and Fraatz to identify specific cells using the time delay integration charge-coupled detector to collect images of cells, since it has been demonstrated as an effective instrument for acquisition of images for cell analysis as shown in Basiji.

Further, the combination of Rosania and Fraatz and Basiji collectively teach all of the claimed elements, the teaching of Basiji performs the same function in combination with the combination of Rosania and Fraatz as taught individually in Basiji, and the results would be highly predictable (Identifying cell in the images that were acquired by a time delay integration charge-coupled detector).

K. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yaroslavsky in view of Fraatz.

As to Claim 28, Yaroslavsky teaches the method of claim 27. However, Yaroslavsky doesn't explicitly teach wherein the single nuclear marker is 7-aminoactinomycin D.

Fraatz teaches using 7-aminoactinomycin D as a maker for imagining samples (**Fraatz, Column 8, Table 1, Table 2, Column 6, lines 1-20**). Fraatz performs analysis for identifying biological activities in specimens (cells). 4). It would have been obvious to one of ordinary skilled in the art at the time of inventions to modify the kit for identifying cells of Yaroslavsky, by using 7-aminoactinomycin D as the nuclear marker as to the teaching of Fraatz. Yaroslavsky and Fraatz are analogous in the art of image based biological analysis. One of ordinary skilled in the art would have been motivated to combine the teachings of Fraatz to the method of Yaroslavsky in order to use the kit for use in a multispectral imaging system to identify a specific cell type of Yaroslavsky to identify specific cells using the nuclear marker, 7-aminoactinomycin D, since it has useful properties (fluorescent dye) that would enable the isolation of cells in the image, as taught by Fraatz.

Further, Yaroslavsky and Fraatz collectively teach all of the claimed elements, the teaching of Fraatz performs the same function in combination with Yaroslavsky as taught individually in Fraatz, and the results would be highly predictable (Identifying cell in the image using the fluorescent dye (7-aminoactinomycin D) as a nuclear maker).

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Cliffel et al. US PGPub 2005/0014129 A1 - Device and methods for detecting the response of a plurality of cells to at least one analyte of interest

Finkbeiner US PGPub 2003/0103662 A1 Robotic microscopy systems

Frost, PGPub 20060029267, Method and apparatus for reading reporter labeled beads

Hansen US PGPub 2003/0202689 A1 Ray-Based Image Analysis For Biological Specimens

Heckman US PGPub 2002/0164063 A1 Method of assaying shape and structural features in cells

Johnson, US PGPub 2003/0048931 A1 Quantification and differentiation of tissue based upon quantitative image analysis

Jorgenson, US PGPub 2004/0218184 Imaging platform for nanoparticle detection applied to SPR biomolecular interaction analysis

Kim et al. US PGPub 2003/0040031 A1 System for monitoring cell motility in real-time

Muraca US PGPub 2003/0049701 A1 Oncology Tissue Microarrays

Ochs, US PGPub 2004/0111220 A1, Methods of decomposing complex data

Tozer, US PGPub 2004/0241759 A1, High throughput screening of libraries

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Jason Heidemann whose telephone number is (571)-270-5173. The examiner can normally be reached on Monday - Thursday/7:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bhavesh Mehta can be reached on 571-272-7453. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 571-273-8300 for After Final communications. TC 2600's customer service number is 571-272-2600.

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/Jason Heidemann/ 10/14/2009
Examiner, Art Unit 2624

/Wenpeng Chen/

Primary Examiner, Art Unit 2624